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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,557	10/03/2005	Christos Tsaklakis	MERCK-2723	3824
23599 7590 11/27/2009 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201				
EXAMINER LOEWY, SUN JAE Y				
ART UNIT		PAPER NUMBER		
1626				
NOTIFICATION DATE		DELIVERY MODE		
11/27/2009		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary

Application No.

10/551,557

Applicant(s)

TSAKLAKIDIS ET AL.

Examiner

SUN JAE Y. LOEWE

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 23, 26, 29-33 and 40-60 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 23, 26, 29-33 and 40-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-508)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ ~~Notice of Informal Patent Application~~
- 6) ☐ Other: _____
- Paper No(s)/Mail Date _____

DETAILED ACTION

1. Claims 1, 23, 26, 29-33 and 40-60 are pending in the instant application. Prosecution is re-opened in view of the petition decision dated September 3, 2009. The restriction requirement between Groups I-III is withdrawn.

Response to Amendment

2. The amendments to the claims filed on December 16, 2008 have been fully considered. The 35 USC 112 1st and 2nd paragraph rejections have been obviated and are thus hereby withdrawn. The double patenting rejection over US 11/575,711 is withdrawn because this copending application has been abandoned.

3. The full scope of claimed compounds has been searched and examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31, 33, 40 and 41 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states “There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue”. The factors are applied below to the instant claims.

The breadth of the claims

The claims are drawn to methods of treatment which generically encompass diseases such as "tumors", ie. cancer.

The nature of the invention

Support for the methods based on the in vitro inhibition Factor Xa.

The state of the prior art/level of ordinary skill/level of predictability

“Cancer” is a broad genus of diseases with extensive variability in etiology and modes of treatment. The state of the art for treating “cancer” is, in general, unpredictable. For example, clinical trials of tyrosine kinase inhibitors in solid tumors have been largely unsuccessful (Madhusudan et al., p. 628).

The amount of direction provided by the inventor/existence of working examples

No working examples are provided in the instant specification. The guidance/direction is limited to the reported in vitro activity of the instantly claimed compounds as inhibitors of Factor Xa.

The quantity of experimentation needed to make or use the invention

In the absence of working examples/direction, enablement rests on the existence of an art recognized predictable correlation between the disclosed activity and the claimed intended use. Evidence suggests that this requirement is not met for the instant case. Consequently, one of ordinary skill is not enabled by the instant disclosure to practice the claimed invention. The amount of experimentation is undue.

5. Claims 40 and 41 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of compounds of Formula I, does not reasonably provide enablement for the preparation of solvates of the compounds of Formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states “There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue”. The factors are applied below to the instant claims.

The breadth of the claims

The claims are drawn to process of using solvates of the compounds of Formula I.

The state of the prior art/level of ordinary skill/level of predictability

The state of the art for preparing polymorphs (including solvates) of a given compound is unpredictable (eg. see Chawla et al., p. 9, 1st and 2nd paragraphs):

- The number or existence of solid forms cannot be predicted.
- The more diligently any system is studied the larger the number of polymorphs discovered

- It is not commonly known in the art, or predictable, how different solid forms are made (Newman et al., p. 898, 2nd column, last paragraph).

The amount of direction provided by the inventor/existence of working examples
No direction or working examples.

The quantity of experimentation needed to make or use the invention
MPEP 2164.01(a) states:

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the evidence regarding each of the above factors (see discussion above), the specification, at the time the application was filed, would not have taught one of ordinary skill in the art how to practice the claimed invention without undue experimentation.

The instant claims *prima facie* lack enablement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim 26 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 and 21-23 of U.S. Patent No. 7,504,500. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons provided below.

Determination of the scope and contents of claims in cited patent.

Process of making a Markush group of compounds which include species within the instant claims.

Ascertaining the differences between instant claims and the claims in the cited patent

The claims in the copending application are drawn to a genus, of which embodiments fall within the scope of the instant claims.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

The embodiments suggest to one of ordinary skill to practice the instant invention. Thus, the instant claims are prima facie obvious over the claims in the cited patent.

7. Claims 1, 23, 26, 29-33 and 40-60 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-36 of copending Application No. 11/576,207. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons provided below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Determination of the scope and contents of claims in cited patent.

Process of making and using Markush group of compounds which include species within the instant claims. A Markush group of compounds which include species within the instant claims.

Ascertaining the differences between instant claims and the claims in the cited patent

The claims in the copending application are drawn to genres, of which embodiments fall within the scope of the instant claims.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

The embodiments suggest to one of ordinary skill to practice the instant invention. Thus, the instant claims are prima facie obvious over the claims in the cited patent.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe/
11-22-2009

/REI-TSANG SHIAO /
Primary Examiner, Art Unit 1628